SiPM characterization for nEXO

PRESENTED BY TIZIANO BUZZIGOLI





n













E_{initial}

 $\mathsf{E}_{\mathsf{final}}$







 $E_{initial} = E_{final} + Q - value$





n















n

















$\overline{\nu} = \nu$

Majorana Particles











Detection of $0\nu\beta\beta$



e-







- next Enriched Xenon Observatory
 - Multi-tonne (5000kg LXe)
 - Low-background
- 90% Xe¹³⁶ enriched liquid xenon
- Time Projection Chamber (TPC)
- SiPMs
- Anode consisting of charge collection tiles













 \leftarrow <u>____</u> \leftarrow \leftarrow \leftarrow \leftarrow Yale





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 $\leftarrow \leftarrow$, _____ Yale

e-



TIME PROJECTION CHAMBER (TPC)
Moore Lab at Yale



Moore Lab's role in nEXO's R&D

- Characterization of the SiPMs that will be used in nEXO
- Comparison of SiPMs manufactured by FBK and Hamamatsu
- Calibration of the SiPMs using radioactive-sources



Moore Lab's role in nEXO's R&D – what we look for



My role as a member of the team



Moore Lab's setup for SiPM testing







Multi-channel analyzer – data acquisition





Multi-channel analyzer





Multi-channel analyzer – data analysis



Pre-amplifier signal

Shaping amplifier signal



Multi-channel analyzer – data analysis





Multi-channel analyzer – data analysis



DIFFERENT DATA SETS NEED DIFFERENT FIT AND ADJUSTMENT PARAMETERS TO BE ANALYZED

Can we fit each waveform and each histogram manually?

SmartGAT Gain Analysis Tool



- Automatic raw MCA data trimming (pedestal and flat trail removal)
- Smart peak fitting
 - Automatic peak edges detection with parameters adjustements
 - Automatic edges correction when find_peaks fails to detect edges
 - Recognition of good vs bad peak fits -> ignore bad gaussian fits
- Automatic peak number and sequence selection for best results
 - Selection of best subgroup of peaks to obtain cleanest gain measurement
- Backup of data for faster further analysis



- *Multiprocessing* (including on Grace High Power Computer)
 - Loading times greatly reduced by increasing number of cores
- Multithreading within multiprocessing



Gain 22.75 ± 0.0003009102094958566



0.50kHz @ 33.600V -> Gain 1548.99 ± 0.0032062140504914636





7.00kHz @ 33.400V -> Gain 1468.66 ± 0.0010223747738837964



0.50kHz @ 33.400V -> Gain 1495.71 ± 0.004892084057948706



7.00kHz @ 31.000V -> Gain 877.69 ± 0.0026151988745905163



Waveform analysis

NEW STRATEGIES FOR GAIN CALCULATION





path = r'/home/tb829/sipm_data/202206[0-1]*/'

example = Gat(path, 'wave*',4.00,debug=False,force=False,notify=False)
Memory usage (traced): 79.65 MB
[01:50:49PM - __init__]: 56 files and 1 voltages loaded



example.eval_gain(4.00,plot=False,find_best=True,fix_params=True)

[02:21:01PM - eval_waveform_func_fit]: Loading from backup file

[02:21:01PM - __peak_filter]: Average peak mu is 198.53943103967774 for 2275261.879714707 and 11460

[02:21:01PM - ___find_best]: Multiprocessing does not support progress bars.

Resulting peaks:

- * 151.5434322003957 ± 0.1024826880262279
- * 233.3873251316392 ± 0.1264417260768181
- * 315.1470115767167 ± 0.3374323933332382
- * 396.8200309403013 ± 0.2084546172419785
- * 478.9852437822216 ± 0.3005449807690225

[02:28:11PM - __gain_from_peaks]: Gain: 69.74 ± 0.08

Memory usage: 478.643887 MB peak

example.eval_gain(4.00,plot=False,find_best=True,fix_params=True)

[02:21:01PM - eval_waveform_func_fit]: Loading from backup file

[02:21:01PM – ___peak_filter]: Average peak mu is 198.53943103967774 for 2275261.879714707 and 11460

[02:21:01PM - ___find_best]: Multiprocessing does not support progress bars.

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- * 233.3873251316392 ± 0.1264417260768181
- * 315.1470115767167 ± 1.3374323933332382
- * 396.8200309403013 -> FIT FAILED
- * 478.9852437822216 ± 0.3005449807690225



example.plot(hist=True, hist_fit=True)



GOOD GAUSSIAN FIT

Vale



example.plot(hist=True, gain=True, hist_fit=True)



GAT





















$$V(t) = V_0 + \frac{A}{2} \cdot \exp\left(\frac{1}{2}\frac{\sigma^2}{\tau^2} - \frac{t-\mu}{\tau}\right) \cdot \operatorname{erfc}\left(\frac{1}{\sqrt{2}}\frac{\sigma}{\tau} - \frac{t-\mu}{\tau}\right)$$



P

Results

FROM SmartGAT


Gain vs Bias voltage analyis pre/post resistor change





Gain vs Bias voltage analyis pre/post resistor change



Yale

Summary and conclusions

- Created a Python class (SmartGAT) that utilizes a smart algorithm to distinguish between waveforms and histograms corresponding to SiPM PEs
- SmartGAT fits single PE histogram peaks from the MCA as well as from raw waveforms from the pre-amplifier
- This tool has enabled quick calculation of SiPM gain which will be utilized by Moore Lab for SiPM characterization such as stability in LXe, electric field as well as exposure to radioactive calibration sources



References

[1] Sensitivity and Discovery Potential of nEXO to Neutrinoless Double Beta Decay - Scientific Figure on ResearchGate. Available from: https://www.researchgate.net/figure/Engineering-design-rendering-of-the-nEXO-experiment-concept-forconcreteness-drawn-in_fig1_320441791 [accessed 17 Aug, 2022]

[2] Characterisation of Silicon Photomultipliers with Xenon Scintillation Light for the nEXO Experiment by Tobias Ziegler (2016)



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Prof. Antonio Ereditato, PhD Victoria Misenti

Taylor Dunnigan





'LET THERE BE LIGHT'

ANTONIO FERRALORO Medical Student University of Messina

ONAOSI-YALE UNDERGRADUATE RESEARCH EXPERIENCE IN INSTRUMENTATION · ·Summer 2022

W right Laboratory, Yale University June 19th - August 20th



Wright Laboratory







DUNE Experiment

. . .



Near Detector

. . .

• • •







What I focused on: LArTPC



The

Cryostat section





Single Cube

105/1

Cryostat

Slow Control

Key components:

. . .

- Temperature sensors
- Pressure gauges
- Pressure valve control
- LAr purity, level and control sensors
- Arduino and LabView Main Display



Arduino UNO REV3 A0006



RTDs



Pressure Gauge

LabView Main Display Poshu Ng





<u>Resistance/Temperature</u> detectors: detect temperature through a change in resistivity of certain materials.

 $ho(T)=
ho_0\cdot [1+lpha(T-T_0)]$

Resistivity/Temperature linear relation Wikipedia



Image of an RTD labfacility.com . . .



RTDs Calibration Experiment

PURPOSES

- RTDs for calibration
- Arduino connections .
- Level sensor.

MATERIALS

- Ice-filled Cooler
- Insulative material
- Wiring for all 5 RTDs
- Thin, non-permeable bags.
- Thermometre



"RTDs Calibration Experiment Setup" Poshu Ng





RTDs Calibration Experiment Results

Consistency vs Accuracy



230 Ohm with 0.0128V offset		Arduino	Difference	
2	229	229.79	-0.79	
3	228.54	228.36	0.18	
4	228.62	228.44	0.18	
5	228.56	228.38	0.18	
9	228.15	227.97	0.18	
			-0.014	

Time

"Temperature over time for 4 RTDs" Matt King

"Test Resistances w/ Voltage Offset" Poshu Ng





Key components:

- ArcLight
- <u>Multi-Pixel Photon Counter (SiPM</u>
- <u>Multi-Channel Front-End Board for</u> <u>SIPM Readout</u>







ArCLight



- A 4mm EJ280 WLS with reflective films
- A dichroic film transparent in blue and reflective in green
- A dielectric specular reflector foil with a 98% reflectance in the visible spectrum [1]



ArCLight Layers [II]





Multi-Pixel Photon Counter



Geiger mode^[2]

- Switch is open
- Cj is charged to bias voltage
- Bias voltage > Breakdown voltage.
- No current flowing

Equivalent circuit of an APD operating in Geiger mode. [III]



Front-End Board

Some of its functions are [3]:

- Amplifies and perform shaping of mppc output on each channel
- Performs digitization of signal amplitude for 32 channels
- Provides basic coincidence of signals from each pair of adjacent channels





DATA COLLECTION AND LIGHT DETECTION TESTS

- Ensure diodes are functioning for all SiPMs
- Create a baseline for all SiPMs
- Collect data for all SiPMs in dark conditions and with light
- Repeat all the steps increasing the bias voltage by 0.1V







LED Driver

114/1





ADC Channel



Data Analysis and Curve fitting Code

pip install scipy

Boort scipy from astropy.modeling.models import Lorentz1D from scipy.optimize import curve_fit

√ 8.2s

Requirement already satisfied: scipy in /opt/anaconda3/lib/python3.9/site-packages (1.7.3) Requirement already satisfied: numpy<1.23.0,>=1.16.5 in /opt/anaconda3/lib/python3.9/site-packages (from scipy) (1.21.5)

filepath_l = "./light_1660242630_Light_56_8V.root" filepath_nl = "./light_1660242376_NoLight_56_8V.root" filepath_lt= "./light_1660242841_LightTrig_56_8V.root"

content_nl = uproot.open(filepath_nl)
content_l = uproot.open(filepath_l)
content_lt=uproot.open(filepath_lt)
print(content_nl.keys())

√ 0.1s

['mppc;1']

data_nl = content_nl["mppc"]
data_l = content_l["mppc"]
data_lt= content_lt["mppc"]
data_nl.show()

√ 0.8s

def _2Lorentzian(x, amp1, cen1, wid1, amp2,cen2,wid2,amp3, cen3, wid3,amp4,cen4,wid4):

return (amp1*wid1**2/((x-cen1)**2+wid1**2)) +\
 (amp2*wid2**2/((x-cen2)**2+wid2**2)) +\
 (amp3*wid3**2/((x-cen3)**2+wid3**2))+\
 (amp4*wid4**2/((x-cen4)**2+wid4**2))

channel_names = [3, 30]

guess=[1600, 210, 10, 400, 370, 15, 400,470, 15,200,580,30]
for i in range(0, 2):
 bins = np.linspace(0, 3000, 500)
 counts, bins = np.histogram(nl_channels[i], bins= bins)
 bin_width = bins[2] - bins[1]
 fig = plt.figure(figsize=(8,6))
 y, b_x,z = plt.hist(bins[:-1], bins, weights=counts/bin_width, histtype="step", color='blue', label='Single Box : '+str(len(nl_channels[i]))+" Events")

#counts, bins = np.histogram(nl_channels[i], bins=bins)
#plt.hist(bins[:-1], bins, weights=counts/bin_width, histtype="step", color='b', label='Double Box: '+str(len(nl_channels[i]))+" Events")

bin_centres = np.array((b_x[:-1] + b_x[1:])/2)

plt.xlabel('\nADC Channel', fontsize=14)
plt.ylabel('Count/Bin Width\n', fontsize=14)
plt.title('Presentation Data ADC for Channel '+str(channel_names[i])+'\nBin Width: '+str(round(bin_width,1))+'\n', fontsize=18)
plt.legend(loc='upper right', fontsize=13)
plt.tight_layout()
plt.xlim(0, 1100)
#plt.yscale('log')

coefficients, var = curve_fit(_2Lorentzian, bin_centres,y,p0= guess, maxfev=2000000)
print(coefficients)
print(np.sqrt(np.diag(var))[1])
lorentzian = _2Lorentzian(bin_centres, *coefficients)
plt.plot(bin_centres, lorentzian, color='lime')
plt.show()

. . .







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. . .

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- **Angela White** and **Matt King**, Phd students at Yale University
- **Poshu Ng**, High School Intern
- The ONAOSI-YALE Programme **Students**



Onaosi-Yale Programme Students







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 Measuring the electrical and optical properties of silicon multipliers
 Multi-channel front-endboard for SiPM readout: M.Auger, A.Ereditato, D. Goeldi, I. Kreslo, M. Luethi, T. Mettler, C. Rudolf von Rohr, J. R. Sinclair, and M.S. Weber

Images

I: Arclight- a compact dielectric Large-Area Photon Detector: M.Auger, Y. Chen, A.Ereditato, D. Goeldi, I. Kreslo, D. Lorca, M. Luethi, T. Mettler, J. R. Sinclair, and M.S. Weber
II: Arclight- a compact dielectric Large-Area Photon Detector: M.Auger, Y. Chen, A.Ereditato, D. Goeldi, I. Kreslo, D. Lorca, M. Luethi, T. Mettler, J. R. Sinclair, and M.S. Weber
III: Measuring the electrical and optical properties of silicon multipliers
IV: Multi-channel front-endboard for SiPM readout: M.Auger, A.Ereditato, D. Goeldi, I. Kreslo, M. Luethi, T. Mettler, C. Rudolf von Rohr, J. R. Sinclair, and M.S. Weber



Advanced Imaging of Brain Tumors

Lodovico Balzoni, Department of Neuroradiology and Nuclear Medicine

August 18th, 2022



Types of classifications







PNETs



Sturm D, Orr BA, Toprak UH, Hovestadt V, Jones DTW, Capper D, et al. New Brain Tumor Entities Emerge from Molecular Classification of CNS-PNETs. Cell. 2016;164:1060-72.

MRI physics



MN1-mutated astroblastoma: case presentation



Healthy, 9 y.o. girl

T1 is used for:







Gadolinium-enhanced T1

T2 is used for:





Anatomic details (CSF)

Most lesions

But it cannot distinguish lesions from CSF

FLAIR is used for:





Lesions near ventricles

Edema



Grey white matter differentiation



FLAIR






DWI-ADC



Tractography







3 years and 6 months after diagnosis

Conclusions and future perspectives



Aggressive features do not necessarily correlate with aggressive behavior.



Histologic and imaging features combined with molecular and epigenetic profiles would allow more clear classification and prognosis, thus favoring individualized therapy.





Last followup case 1



Case 2









Case 3



Last followup case 3



Case 4





Last followup case 5



Conclusions

- Not all PNETs are the same and current classification of brain tumors requires better understanding of imaging features;
- PNETs are a specific subtype of brain tumors that are now classified based on epigenetic modificination but mutations play a role in classes such MN1 mutation;
- GBMs with PNET features have specific imaging features which may help in suggesting diagnosis;
- Gross total resection is the most important factor in predicting prognosis.

Introduction to Synthetic MRI



Figures adapted from:

Gonçalves, F. G., Serai, S. D., & Zuccoli, G. (2018). Synthetic brain MRI: Review of current concepts and future directions. In Topics in Magnetic Resonance Imaging (Vol. 27, Issue 6, pp. 387–393). Lippincott Williams and Wilkins. Ji, S., Yang, D., Lee, J., Choi, S. H., Kim, H., & Kang, K. M. (2020). Synthetic MRI: Technologies and Applications in Neuroradiology. In *Journal of Magnetic Resonance Imaging*. John Wiley and Sons Inc.

Data analysis

	Standard sequences	STAGE sequences
Number of cases where <u>Swallow tail sign</u> is visible	2/18 bilateral 2/18 unilateral	17/21 2/21 bilateral
Number of cases where <u>Subthalamic nucleus</u> is visible	3/18	19/21
Number of cases where <u>T1</u> <u>sequence</u> was preferred	8/21	13/21
Number of cases where <u>T2</u> <u>sequence</u> was preferred	21/21	0/21
Number of cases where <u>SWI</u> <u>sequences</u> was preferred	0/21	21/21
Number of <u>microbleeds</u> reported	3/21	21/21

Conclusions

Patients need uniform and rapid imaging protocols for standardization of features extraction:

- Highly variable protocols in clinical practice prevent innovation in fields such as AI;
- STAGE is a consistent and rapid way of acquiring sequences, although improvements are necessary to allow clinical use.

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MRI physics video is taken from: <u>https://www.nibib.nih.gov/science-education/science-topics/magnetic-resonance-imaging-mri</u> Papilledema picture is taken from: <u>https://www.ophthalmologyreview.org/articles/papilledema</u> Brain images are taken from: <u>https://radiopaedia.org</u>

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Tayor Dunningan Victoria Misenti





New Frontiers in CNS neoplasms classification and diagnosis: The Role of Neuro-Imaging

Francesca Conti, Department of Neuroradiology and Nuclear Medicine August 18th, 2022



WHO Classification of Tumours of the Central Nervous System

2007

World Health Organization Classification of Tumours



Pathology & Genetics

Tumours of the Nervous System

Edited by Paul Kleihues & Webster K. Cavenee







2016

WHO Classification of Tumours of the Central Nervous System

Deald H. Louis, Hindu Digali, Olmar D. Wastier, Weinder K. Cavanas, David W. Ellison, Boninique Figurale-Onunger, Arie Party, Guide Fallerbarger, Ambrass von D





















WHO Classification of Tumours • 5th Edition

Central Nervous System Tumours

Edited by the WHO Classification of Tumours Editorial Board















onal Agency for Research on Cance World Health



Can Neuro-Imaging provide a better understanding of CNS tumors?

Case Report

- Analysis of a rare brain tumor case
- Search for unique imaging features that could help in diagnosis and classification

Image - Based Search

- Development of an algorithm that permits an image-based search in the hospital database
- Creation of tumor clusters based on imaging
- Analysis of results



Lymphomatoid Granulomatosis

- Lymphomatoid Granulomatosis (LYG) is a rare lymphoproliferative disease.
- While details behind the pathogenesis of LYG remain unknown², it has been proven to follow a previous EBV infection³.
- The pathological damage is caused by rapid expansion of lymphocyte clones, most frequently of a B-cell phenotype³⁻⁵.
- \circ A T-cell phenotype is also possible, particularly in HIV-infected patients³⁻⁵.



LYG most commonly originates in the lungs with subsequent systemic involvement of skin and CNS^{1,2,4-6.}

Rare instances of primary CNSLYGhavealsobeendocumented in the literature10





LYG





Vasculitis

Primary differential diagnosis^{3,8,11}:

- Primary CNS Lymphoma Ο
- **CNS** vasculitis 0

Neurological symptoms at presentation^{3,6,8,11}:

- dizziness 0
- dysarthria 0
- lower limb numbness Ο
- involuntary movement Ο
- headaches 0
- parkinsonism Ο

LYG grading is based on the predominant lymphocyte phenotype, the amount of necrosis and the amount of EBV infected cells.

The higher the number of EBV+ cells, necrosis and proliferation, the higher the grade of LYG will be.



Common treatment options for CNS LYG include chemotherapy, radiotherapy, steroids, surgical resections and anti-retroviral treatment for HIV patients; however, a standardized treatment scheme has not yet been developed^{2,3,10,14}.







Our cohort of LYG patients consisted of more than 90 patients. Five of them had central nervous system involvement.



We built a case report of one of those cases.

Primary CNS Lymphomatoid Granulomatosis

The patient is a 48 year-old man, HIV and HBV positive, with poly-substance abuse history. He was admitted because of refractory seizures and was started with fosphenytoin and Keppra, but the seizures continued with progressive decline in mental status despite treatment.





Imaging - First Set of Scan from an Outside Facility



Gadolinium - enhancing T1

Imaging - First Set of Scan from an Outside Facility



Imaging - Follow up Scan from Yale Health



Gadolinium - enhancing T1
Imaging - Follow up Scan from Yale Health



Imaging - Follow up Scan from Yale Health



Imaging - Follow up Scan from Yale Health



Histopathology

Haematoxylin and Eosin stain

In-situ hybridization (ISH) EBV





EBV role



- First encounter and primary infection
- $\circ\,$ Primary infection resolution
- $\,\circ\,$ Latency inside B lymphocytes
- T-cells (CD4+/CD8+) control B-cell

proliferation

- Immunocompromised status can lead to
 EBV+ cells proliferation
- Possible malignant transformation

HIV and immunodeficiency role

- HIV targets CD4+ T-cells
- HIV+ patients have a higher chance to develop lymphoproliferative diseases
- CNS-LYG HIV+ patients show a predominant T-cell infiltrate
- In HIV+ patients, the disease is more aggressive





Imaging at diagnosis

Follow-up diagnosis





HAART Therapy (Dolutegravir and TRUVADA)

Dexamethasone: 4 milligrams every 8 hours for two weeks

Discharged

 \circ Lost at follow-up



Median survival rate of 2 years $\frac{16}{16}$

Systemic LYG without CNS involvement has a 66% mortality rate at 14 months⁷

Systemic LYG with CNS involvement has a median mortality rate of 86% at 14 months⁷

Primary CNS LYG correlates with a better life expectancy than systemic LYG^{3,7,9}

Image - Based Search



What happens when radiologist are unsure about a diagnosis?





What if we used the hospital dataset?

- The Picture Archiving and Communication System (PACS) in large hospitals contain thousands of cancer images associated with valuable clinical and pathology data.
- When reading a new patient with brain tumor, finding similar images within PACS can help to generate a differential diagnosis.



We propose an 'image-based' search workflow that uses autosegmentation and automated feature extraction to serve as diagnostic aid

We developed tools to automatically segment tumors and extract features in user interfaces that work within our PACS

How does it work?







Meningiomas

- Case retrieval from 2020 and 2021 tumor boards
- Manual segmentation
- \circ Creation of the different cohorts:
 - Typical meningiomas
 - Atypical meningiomas



- Differential diagnosis assistance
- Annotation of imaging data to build databases
- Radiology Education
- $\circ~$ Image based tumor classification



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ImmunoPET: Towards non-invasive selection of lung cancer patients for antibody therapies

Margherita Montavoci

Marquez-Nostra Laboratory of Cancer Imaging and Therapeutics



18th August 2022

Projects







Background Information: Unmet Need

Non-small Cell Lung Cancer

- Epidemiology
 - 2,206,771 lung cancer diagnoses in 2020
 - 82% is NSCLC
- Current therapeutics • EGFR-targeted drugs
 - Develop resistance after 1 year



Lung Cancer - Non-Small Cell - Statistics https://www.cancer.net/cancer-types/lung-cancer-non-small-cell/statistics

Illustration available from: Types of Non-Small Cell Lung Cancer: Causes, Treatment, and Outlook https://www.healthline.com/health/lung-cancer/types-of-non-small-cell-lung-cancer





Background Information: Treatment regimes

- CHRYSALIS (net

24

Monthe

8.3 (6.5, 10.9) 0.47 (0.34, 0.6)

FDA-approved Amivantamab (targets <u>Epidermal Growth Factor Receptor and</u> <u>cytoplasmic Mesenchymal Epithelial Transition</u>)

A Progression-free survival

41

0.00

CHRYSALIS (n=81)

Number at risk



The overall response rate is 40%.

Minchom, A.; Viteri, S.; Bazhenova, L.; Gadgeel, S. M.; Ou, S.-H. I.; Trigo, J.; Bauml, J. M.; Backenroth, D.; Bhattacharya, A.; Li, T.; Mahadevia, P.; Girard, N. Amivantamab Compared with Real-World Therapies in Patients with Advanced Non-Small Cell Lung Cancer Harboring EGFR Exon 20 Insertion Mutations Who Progressed after Platinum-Based Chemotherapy. *Lung Cancer* **2022**, *168*, 74–82. https://doi.org/10.1016/j.lungcan.2022.03.005.





Current Selection Methods

- Biopsy
 - Immunohistochemistry (IHC)
 - Fluorescence In Situ Hybridization (FISH)
 - Gene Mutation Testing
- Limitations of tissue-based analysis:
 - Small sampling
 - Difficult to quantify heterogeneity
- Need a whole-body assessment



Marchio C. et al. 2020. Seminars in Cancer Biology





Positron Emission Tomography (PET)



Videos available from: https://gfycat.com/selfassuredremorsefuldrever-positron-emission-tomography-diagnostic-test





PET Imaging







Zirconium-89

- ⁸⁹Zr half-life matches biological half-life of antibodies
- Ideal for ImmunoPET
- Increased tumor to background ratio due to:
 - Extended imaging time
 - Residualizing property

$$89^{69}Zr \qquad t_{1/2} = 78.41 \text{ h}$$

$$22.3\% \beta^{+}$$

$$76.6\% \text{ EC}$$

$$t_{1/2} = 15.66 \text{ s}$$

$$100\% 909.9 \text{ kEV}$$

$$89^{9}Y$$





Designing ImmunoPET Agents: ⁸⁹Zr-AMI-DFO







Designing ImmunoPET Agents: ⁸⁹Zr-AMI-DFO





Tumor-associated protein target Cell surface proteins (EGFR and cMET)

Targeting vector Amivantamab (targeting EGFR and cMET)

Bifunctional Radiometal metal chelate 89Zr Desferrioxamine (DFO)





Designing ImmunoPET Agents: ⁸⁹Zr-AMI-DFO

- 1. Radiolabeling of AMI-DFO with ⁸⁹Zr
 - pH 6.8-7.2
 - Room temperature
- 2. Characterization of ⁸⁹Zr-AMI
 - Radio-Thin Layer Chromatography
 - High Performance Liquid Chromatography











ImmunoPET for patient selection







PET Imaging and Treatment Paradigm


Baseline CT/PET Imaging







Tumor Growth Curve







Tumor Growth Inhibition



$$\% TGI = \left(1 - \frac{RTV_{treated group}}{RTV_{control group}}\right) \times 100(\%)$$

$$RTV = \frac{tumor \ volume \ _{day \ 25}}{tumor \ volume \ _{day \ 0}}$$





Baseline and post therapy comparison







HOOL OF MEDICINE

Maximum Intensity Projections







HOOL OF MEDICINE

Tumor-to-heart SUV ratios

15₇ Baseline Post AMI Mean T/H SUVs 10activity in tissue SUV =– × mass 5 injected activity mean SUV_{tumor ROI} 0 M21201 M21203 M21205 M21206 M21208 M21209 SUV ratio = mean SUV_{heart ROI} Patient ID

HCC827 Tumor/Heart SUVs





Learning Outcomes

- Interdisciplinary lab
- Team working in research
- Practical aspects of working in a lab



• A priceless opportunity to confirm my interest in research

Tumor/cell biology





Instrumentation







Softwares for image and data analysis











HOOL OF MEDICINE

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Prostate NLG diffusion phantom using PVP water solution

- Andrea De Simone



First, some questions

- What is diffusion?
- What is a non-linear gradient (NLG)?
- What is a phantom?









Diffusion-weighted imaging

• Diffusion-weighted imaging (DWI) is a form of MR imaging based upon measuring the random Brownian motion of water molecules within a voxel of tissue.



From DWI to ADC maps







How does MRI work?





Larmor frequency: $\omega = -\gamma B$

Diffusion weighting (without diffusion)





Maximum signal

Diffusion weighting (with diffusion)



- Spins *approximately* return to x-axis
- But not perfectly aligned
- Pixel gets darker!

LOSS OF SIGNAL





 \uparrow randomization of direction = \uparrow signal loss = \uparrow sensitivity to diffusivity

What is a gradient in DWI?

- $S = S_o e^{-bD}$
- $b = \gamma^2 G^2 \delta^2 (\Delta \delta/3)$



Stronger gradient

Better image

The benefits of NLGs





- Concentrates the field change
- Works well on the prostate (small, close to surface, relatively isotropic).
- High SNR
- "[...] Shorter <u>encoding times and</u> <u>higher b-values increase the</u> <u>ability to distinguish benign and</u> <u>cancerous lesions</u>".¹

Let's compare

T2w Anatomical Reference



Apparent Diffusion Coefficient (ADC) Map



Our NLG



 The magnetic field is created right in front of the prostate, allowing for a much stronger gradient in our ROI.



Our NLG hardware











What is a phantom?

 A phantom is a specially designed object that is utilized as a "stand-in" for human tissue and can be scanned or imaged to evaluate, analyze, and fine-tune the performance of an imaging device.



Okay...

...now what?



The purpose of our study



• To validate the feasibility and accuracy of DWI and ADC mapping using NLGs [that are] designed to provide a high gradient at the prostate.¹

• [This] could help distinguish between malignant and benign prostate lesions, thereby saving patients from unnecessary invasive procedures such as biopsies.²



Step 1: designing the phantom

- The phantom was designed in two parts.
- 1) First, the **arch-like structure** was created to fit the gradient coil.
- 2) Additionally, we designed a **box** that could hold the six PVP vials plus a distilled water vial.
- Easier to switch between phantoms!







Step 2: PVP water solution



 In order to replicate and mimic the prostate tissue, we decided to use a PVP water solution with different PVP concentrations.³





Final result!





Step 3: scanning the phantom



What we were expecting...



Pierpaoli et al. (2009), 1414



...what we got







- The non-linear gradient coil produced similar diffusivity results with different PVP concentrations to those produced using the linear gradient coil.
- Future work will demonstrate accuracy gains obtainable from shorter diffusion encoding times.





- ¹ Hoque Bhuiyan et al., 2021 Oct;48(10):5804-5818. doi: 10.1002/mp.15100
- ² Bauer et al., 87:1605-1612.https://doi.org/10.1002/mrm.29043
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The role of physical exercise in Parkinson's disease: A clinical, radiological, and wearable tools analysis

Giulia Colonna,

Advanced Modeling Laboratory,

Yale PET Center,

Department of Radiology and Biomedical Imaging.





Background

Parkinson's Disease:

- <u>Epidemiology:</u>
 - Second most common neurodegenerative disorder in US
 - o 60,000 new cases per year
- <u>Pathology:</u>
 - Degeneration of dopamine-producing neurons in the substantia nigra (SN) pars compacta.
- <u>Symptoms:</u>
 - Resting tremor
 - Rigidity
 - o Bradykinesia
 - Postural instability.



SUBSTANTIA NIGRA Translated literally as 'black substance'. Loss of dopaminergic neurones here responsible for Parkinson's.

https://app.pulsenotes.com/medicine/neurology/notes/parkinson-s-disease





Treatment of Parkinson Disease:

- Levodopa
- Carbidopa
- MAO-B inhibitors
- Dopamine agonists
- Amantadine



Parkinson's Disease and Exercise:



Effectiveness of home-ba supervised aerobic exercis double-blind, randomised

Nicolien M van der Kolk¹ Nienke M de Vries¹

Nonpharmacological treatments for patients with Parkinson's disease

Bastiaan R Bloem ¹, Nienke M de Vries ¹, Georg Ebersbach ²

<u>**Purpose of the study</u>**: potential neuroprotective effects of high-intensity exercise in humans with PD using multimodal neuroimaging techniques.</u>

Boxing training for
a case seriesSymptoms in Patients With De Novo ParkinsonDisease: A Phase 2 Randomized Clinical Trial

Stephanie A Combs ¹, M Dyer Diehl Katie Schaneman Margaret Schenkman¹, Charity G Moore², Wendy M Kohrt³, Deborah A Hall⁵, Anthony Delitto⁶, Cynthia L Comella⁵, Deborah A Josbeno², Cory L Christiansen¹⁴, Brian D Berman⁷, Benzi M Kluger⁷, Edward L Melanson⁴⁸, Samay Jain⁹, Julie A Robichaud¹⁰, Cynthia Poon¹¹, Daniel M Corcos¹²

Imaging study Methods:





- The MRI will be used to assess **dopaminergic degeneration**, by targeting neuromelanincontaining neurons.
- NM can be measured accurately with MRI due to its ferromagnetic properties







- The PET will be used to assess **the functionality of the dopaminergic system** by targeting the dopamine transporter **(DAT)**.
- novel radioligand [18F]FE-PE2I



Dopamine transporter imaging with [18F]FE-PE2I PET and [123I]FP-CIT SPECT—a clinical comparison, Susanna J.

Patient Cohort and Study Design :



6

11 (6M, 5F) eligible subjects with PD defined according to the Movement Disorder Society (**MDS**)

- Clinical evaluation (H&Y scale)
- Motor function tests (UPDRS)
- Baseline NM-MRI
- [18F]FE-PE2I PET scan

- Clinical evaluation (H&Y scale)
- Motor function tests (UPDRS)
- NM-MRI
- [18F]FE-PE2I PET scan



4

Beat PD Today

- The Beat PD Today project:
 - Individualized High-intensity training
 Boxing
 - \circ 1h session 3 times/week
- HR Tracking devices:

 \circ Fitbit

 \odot PolarH10 + HRVelite chest strap

- Parameters:
 - 70/80 % of maximum HR
 - High intensity Heart Zone (70%-85% of Heart Reserve)





Why two devices?



HRV polar:

- Measures the myocardial electric potentials (= electrocardiogram)
- Correlation with ECG: *r*=0.997³
- Discomfort and complex interface



Fitbit Charge 4 :

- Measures the volume changes in blood vessels throughout a PPG optical heart-rate sensor.
- Previous models underestimate HR measurments of an average of 6bpm at baseline and 16 bpm at higher HR.⁴
- Confortable and convenient



PolarH10 heart rate monitor vs Fitbit: A validation study in PD patients



PolarH10 heart rate monitor vs Fitbit: A validation study in PD patients

To evaluate the **feasibility of Fitbit Charge 4 in measuring HR** compared to HRV polar Heart rate monitor.

Methods

Data Analysis :







Data Analysis :





Data Analysis :

Calculated values :

subjects,

compare



```
for one_df in groups:
                                                                     one_df.set_index('Time', inplace = True)
                                                                     a =one_df['HR_(BPM)'].resample('1T').mean()
                                                                     print(a)
                                                                    #calculating statistics:

    Time frame: 01/01/2021 – 08/06/2022

                                                                    patient1=pd.DataFrame(columns = ['baseline_avg', 'total_avg', 'max_avg'])
                                                                    for ii, one df in enumerate(groups):
                                                                     baseline_avg=[(one_df['HR_(BPM)'].iloc[0:5]).mean()]
     Number of subjects: 10
                                                                     total_avg=[(one_df['HR_(BPM)']).mean()]
                                                                     print(baseline avg)
  • Session average duration: 1h
                                                                     print(total_avg)
                                                                     i = 0
                                                                     highest_avg = []
                                                                     while i < len(one_df)-20:</pre>
                                                                        highest_avg.append([(one_df['HR_(BPM)'].iloc[i:i+20]).mean()])
        • Baseline AVG (<5min)
                                                                        i += 1
                                                                     max_avg = max(highest_avg)
                                                                     patient1 = patient1.append(pd.Series([baseline_avg,total_avg,max_avg], index=['baseline_avg
        • Highest AVG (20 min)
                                                                     #filtering the Fibit file with the sessions Date and Time (from HRV):
                                                                     y=range(len(df))
                                                                     #y=range(60)
                                                                     options3=df['new date']
                                                                     options2 = df['new time'].dt.round('1min')
                                                                     NewFitbit df.reset index(inplace=True)
                                                                     results=[]
                                                                     for x in y:
                                                                         options4 = [options2[x]]
30 paired session (2,5 months) from each
                                                                         options5 = [options3[x]]
                                                                         NewFitbit_df['time1'] = NewFitbit_df['Time'].dt.round('1min')
                                                                         NewFitbit2 df=NewFitbit df['time1'].isin(options4) NewFitbit df['Date'].is.
                                                                         results.append(NewFitbit2 df)
for a total 300 calculated values to
                                                                     #indexes of the starting time:
                                                                     results= pd.concat(results)
                                                                     #print(results['Date'].unique)
                                                                     filtered_date=results['Date'].unique()
```

















Between-subjects variability :

Subject:	Baseline Difference (bpm) :	Highest AVG Difference (bpm) 💂
Subject 1	1,55	-6,46
Subject 2	-2,86	-8,16
Subject 3	1,77	6,65
Subject 4	-0,69	-7,84
Subject 5	-1,09	-12,15
Subject 6	2,05	-7,97
Subject 7	-6,59	9,03
Subject 8	-10,95	-9,26
Subject 9	-0,58	-10,85
Subject 10	-2,47	-6,81

Conclusions:

- Baseline condition = + **1,84 bpm**
- High intensity exercise = + 6,13 bpm
- Fitbit accuracy is HR-dependent, and there is a high between-subjects variability
- A larger study could be conducted just using the Fitbit

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